

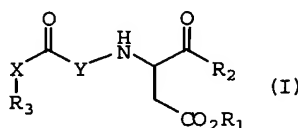


### *Amendments to the Claims*

The listing of claims will replace all prior versions, and listings of claims in the application.

Claims 1-83 (canceled).

Claim 84 (new). A method of treating or ameliorating cell death in lupus erythematosus, rheumatoid arthritis or type I diabetes, comprising administering to an animal in need of such treatment or ameliorating an effective amount of a compound having the Formula I:



or pharmaceutically acceptable salts or prodrugs thereof, wherein:

R<sub>1</sub> is an optionally substituted alkyl or hydrogen;

R<sub>2</sub> is hydrogen or optionally substituted alkyl;

R<sub>3</sub> is an alkyl, saturated carbocyclic, partially saturated carbocyclic, aryl, saturated heterocyclic, partially saturated heterocyclic or heteroaryl group, wherein said group is optionally substituted;

X is O, S, NR<sub>4</sub> or (CR<sub>4</sub>R<sub>5</sub>)<sub>n</sub>, where R<sub>4</sub> and R<sub>5</sub> are, at each occurrence, independently selected from the group consisting of hydrogen, alkyl and cycloalkyl, and n is 0, 1, 2 or 3; or

X is NR<sub>4</sub>, and R<sub>3</sub> and R<sub>4</sub> are taken together with the nitrogen atom to which they are attached to form a saturated heterocyclic, partially saturated heterocyclic or heteroaryl group, wherein said group is optionally substituted; or

X is CR<sub>4</sub>R<sub>5</sub>, and R<sub>3</sub> and R<sub>4</sub> are taken together with the carbon atom to which they are attached to form a saturated carbocyclic, partially saturated carbocyclic, aryl, saturated heterocyclic, partially saturated heterocyclic or oxygen-containing heteroaryl group, wherein said group is optionally substituted; and

Y is a residue of a natural or non-natural amino acid;

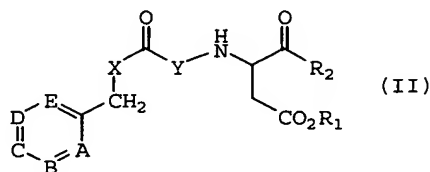
provided that when X is O, then R<sub>3</sub> is not unsubstituted benzyl or *t*-butyl; and when X is CH<sub>2</sub>, then R<sub>3</sub> is not hydrogen.

Claim 85 (new). The method of claim 84, wherein said cell death is due to type I diabetes.

Claim 86 (new). The method of claim 84, wherein said cell death is due to lupus erythematosus.

Claim 87 (new). The method of claim 84, wherein said cell death is due to rheumatoid arthritis.

Claim 88 (new). A method of treating or ameliorating cell death in lupus erythematosus, rheumatoid arthritis or type I diabetes, comprising administering to an animal in need of such treatment or ameliorating an effective amount of a compound having the Formula II:



or pharmaceutically acceptable salts or prodrugs thereof wherein:

R<sub>1</sub> is an optionally substituted alkyl or hydrogen;

R<sub>2</sub> is hydrogen or optionally substituted alkyl;

X is O, S, NR<sub>4</sub> or (CR<sub>4</sub>R<sub>5</sub>)<sub>n</sub>, wherein R<sub>4</sub> and R<sub>5</sub> are, at each occurrence, independently selected from the group consisting of hydrogen, alkyl, and cycloalkyl, and n is 0, 1, 2 or 3;

Y is a residue of a natural or non-natural amino acid;

A is CR<sub>6</sub> or nitrogen;

B is CR<sub>7</sub> or nitrogen;

C is CR<sub>8</sub> or nitrogen;

D is CR<sub>9</sub> or nitrogen;

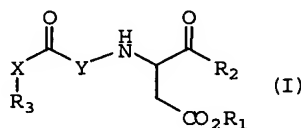
E is CR<sub>10</sub> or nitrogen; provided that not more than three of A, B, C, D and E are nitrogen; and R<sub>6</sub>-R<sub>10</sub> independently are hydrogen, halo, C<sub>1</sub>-C<sub>6</sub> haloalkyl, C<sub>6</sub>-C<sub>10</sub> aryl, C<sub>4</sub>-C<sub>7</sub> cycloalkyl, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>2</sub>-C<sub>6</sub> alkenyl, C<sub>2</sub>-C<sub>6</sub> alkynyl, C<sub>6</sub>-C<sub>10</sub> aryl(C<sub>1</sub>-C<sub>6</sub>)alkyl, C<sub>6</sub>-C<sub>10</sub> aryl(C<sub>2</sub>-C<sub>6</sub>)alkenyl, C<sub>6</sub>-C<sub>10</sub> aryl(C<sub>2</sub>-C<sub>6</sub>)alkynyl, C<sub>1</sub>-C<sub>6</sub> hydroxyalkyl, nitro, amino, cyano, C<sub>1</sub>-C<sub>6</sub> acylamino, hydroxy, C<sub>1</sub>-C<sub>6</sub> acyloxy, C<sub>1</sub>-C<sub>6</sub> alkoxy, alkylthio, or carboxy; or one of R<sub>6</sub> and R<sub>7</sub>, or R<sub>7</sub> and R<sub>8</sub>, or R<sub>8</sub> and R<sub>9</sub>, or R<sub>9</sub> and R<sub>10</sub> are taken together with the carbon atoms to which they are attached to form a carbocycle or heterocycle, selected from the group consisting of —OCH<sub>2</sub>O—, —OCF<sub>2</sub>O—, —(CH<sub>2</sub>)<sub>3</sub>—, —(CH<sub>2</sub>)<sub>4</sub>—, —OCH<sub>2</sub>CH<sub>2</sub>O—, —CH<sub>2</sub>N(R<sub>13</sub>)CH<sub>2</sub>—, —CH<sub>2</sub>CH<sub>2</sub>N(R<sub>13</sub>)CH<sub>2</sub>—, —CH<sub>2</sub>N(R<sub>13</sub>)CH<sub>2</sub>CH<sub>2</sub>—, —N(R<sub>13</sub>)—CH=CH—, —CH=CH—N(R<sub>13</sub>)—, —O—CH=CH—, —CH=CH—O—, —S—CH=CH—, —CH=CH—S—, —N=CH—CH=CH—, —CH=N—CH=CH—, —CH=CH—N=CH—, —CH=CH—CH=N—, —N=CH—CH=N—, and —CH=CH—CH=CH—; wherein R<sub>13</sub> is hydrogen, alkyl or cycloalkyl; provided that when X is O, A is CR<sub>6</sub>, B is CR<sub>7</sub>, C is CR<sub>8</sub>, D is CR<sub>9</sub> and E is CR<sub>10</sub>, then at least one of the R<sub>6</sub>-R<sub>10</sub> is not hydrogen.

Claim 89 (new). The method of claim 88, wherein said cell death is due to type I diabetes.

Claim 90 (new). The method of claim 88, wherein said cell death is due to lupus erythematosus.

Claim 91 (new). The method of claim 88, wherein said cell death is due to rheumatoid arthritis.

Claim 92 (new). A method of protecting a mammalian organ or tissue from cell death due to deprivation of normal blood supply, comprising contacting said organ or tissue with an effective amount of a compound having the Formula I:



or pharmaceutically acceptable salts or prodrugs thereof, wherein:

R<sub>1</sub> is an optionally substituted alkyl or hydrogen;

R<sub>2</sub> is hydrogen or optionally substituted alkyl;

R<sub>3</sub> is an alkyl, saturated carbocyclic, partially saturated carbocyclic, aryl, saturated heterocyclic, partially saturated heterocyclic or heteroaryl group, wherein said group is optionally substituted;

X is O, S, NR<sub>4</sub> or (CR<sub>4</sub>R<sub>5</sub>)<sub>n</sub>, where R<sub>4</sub> and R<sub>5</sub> are, at each occurrence, independently selected from the group consisting of hydrogen, alkyl and cycloalkyl, and n is 0, 1, 2 or 3; or

X is NR<sub>4</sub>, and R<sub>3</sub> and R<sub>4</sub> are taken together with the nitrogen atom to which they are attached to form a saturated heterocyclic, partially saturated heterocyclic or heteroaryl group, wherein said group is optionally substituted; or

X is CR<sub>4</sub>R<sub>5</sub>, and R<sub>3</sub> and R<sub>4</sub> are taken together with the carbon atom to which they are attached to form a saturated carbocyclic, partially saturated carbocyclic, aryl, saturated heterocyclic, partially saturated heterocyclic or oxygen-containing heteroaryl group, wherein said group is optionally substituted; and

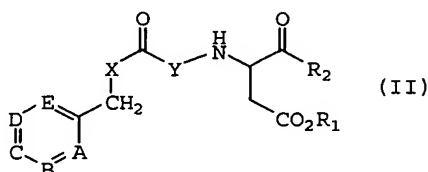
Y is a residue of a natural or non-natural amino acid;

provided that when X is O, then R<sub>3</sub> is not unsubstituted benzyl or *t*-butyl; and when X is CH<sub>2</sub>, then R<sub>3</sub> is not hydrogen.

Claim 93 (new). The method of claim 92, wherein said organ or tissue is present in a storage medium prior to transplant into a mammal.

Claim 94 (new). The method of claim 93, wherein said contacting comprises infusion of said compound into the organ or tissue, or bathing of said organ or tissue in a storage medium which comprises said compound.

Claim 95 (new). A method of protecting a mammalian organ or tissue from cell death due to deprivation of normal blood supply, comprising contacting said organ or tissue with an effective amount of a compound having the Formula II:



or pharmaceutically acceptable salts or prodrugs thereof wherein:

R<sub>1</sub> is an optionally substituted alkyl or hydrogen;

R<sub>2</sub> is hydrogen or optionally substituted alkyl;

X is O, S, NR<sub>4</sub> or (CR<sub>4</sub>R<sub>5</sub>)<sub>n</sub>, wherein R<sub>4</sub> and R<sub>5</sub> are, at each occurrence, independently selected from the group consisting of hydrogen, alkyl, and cycloalkyl, and n is 0, 1, 2 or 3;

Y is a residue of a natural or non-natural amino acid;

A is CR<sub>6</sub> or nitrogen;

B is CR<sub>7</sub> or nitrogen;

C is CR<sub>8</sub> or nitrogen;

D is CR<sub>9</sub> or nitrogen;

E is CR<sub>10</sub> or nitrogen; provided that not more than three of A, B, C, D and E are nitrogen; and R<sub>6</sub>-R<sub>10</sub> independently are hydrogen, halo, C<sub>1</sub>-C<sub>6</sub> haloalkyl, C<sub>6</sub>-C<sub>10</sub> aryl, C<sub>4</sub>-C<sub>7</sub> cycloalkyl, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>2</sub>-C<sub>6</sub> alkenyl, C<sub>2</sub>-C<sub>6</sub> alkynyl, C<sub>6</sub>-C<sub>10</sub> aryl(C<sub>1</sub>-C<sub>6</sub>)alkyl, C<sub>6</sub>-C<sub>10</sub> aryl(C<sub>2</sub>-C<sub>6</sub>)alkenyl, C<sub>6</sub>-C<sub>10</sub> aryl(C<sub>2</sub>-C<sub>6</sub>)alkynyl, C<sub>1</sub>-C<sub>6</sub> hydroxyalkyl, nitro, amino, cyano, C<sub>1</sub>-C<sub>6</sub> acylamino, hydroxy, C<sub>1</sub>-C<sub>6</sub> acyloxy, C<sub>1</sub>-C<sub>6</sub> alkoxy, alkylthio, or carboxy; or

one of R<sub>6</sub> and R<sub>7</sub>, or R<sub>7</sub> and R<sub>8</sub>, or R<sub>8</sub> and R<sub>9</sub>, or R<sub>9</sub> and R<sub>10</sub> are taken together with the carbon atoms to which they are attached to form a carbocycle or heterocycle, selected from the group consisting of —OCH<sub>2</sub>O—, —OCF<sub>2</sub>O—,

—(CH<sub>2</sub>)<sub>3</sub>—, —(CH<sub>2</sub>)<sub>4</sub>—, —OCH<sub>2</sub>CH<sub>2</sub>O—, —CH<sub>2</sub>N(R<sub>13</sub>)CH<sub>2</sub>—,

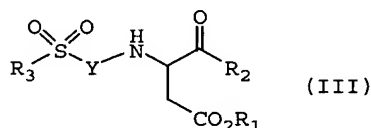
—CH<sub>2</sub>CH<sub>2</sub>N(R<sub>13</sub>)CH<sub>2</sub>—, —CH<sub>2</sub>N(R<sub>13</sub>)CH<sub>2</sub>CH<sub>2</sub>—, —N(R<sub>13</sub>)—CH=CH—, —CH=CH—N(R<sub>13</sub>)—, —O—CH=CH—, —CH=CH—O—, —S—CH=CH—, —CH=CH—S—,

—N=CH—CH=CH—, —CH=N—CH=CH—, —CH=CH—N=CH—, —CH=CH—CH=N—, —N=CH—CH=N—, and —CH=CH—CH=CH—; wherein R<sub>13</sub> is hydrogen, alkyl or cycloalkyl; provided that when X is O, A is CR<sub>6</sub>, B is CR<sub>7</sub>, C is CR<sub>8</sub>, D is CR<sub>9</sub> and E is CR<sub>10</sub>, then at least one of the R<sub>6</sub>-R<sub>10</sub> is not hydrogen.

Claim 96 (new). The method of claim 95, wherein said organ or tissue is present in a storage medium prior to transplant into a mammal.

Claim 97 (new). The method of claim 96, wherein said contacting comprises infusion of said compound into the organ or tissue, or bathing of said organ or tissue in a storage medium which comprises said compound.

Claim 98 (new). A method of protecting a mammalian organ or tissue from cell death due to deprivation of normal blood supply, comprising contacting said organ or tissue with an effective amount of a compound having the Formula III:



or pharmaceutically acceptable salts or prodrugs thereof, wherein:

R<sub>1</sub> is an optionally substituted alkyl or hydrogen;

R<sub>2</sub> is hydrogen or optionally substituted alkyl;

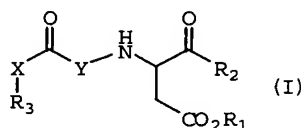
R<sub>3</sub> is an alkyl, saturated carbocyclic, partially saturated carbocyclic, aryl, saturated heterocyclic, partially saturated heterocyclic or heteroaryl group, wherein said group is optionally substituted; and

Y is a residue of a natural or non-natural amino acid.

Claim 99 (new). The method of claim 98, wherein said organ or tissue is present in a storage medium prior to transplant into a mammal.

Claim 100 (new). The method of claim 99, wherein said contacting comprises infusion of said compound into the organ or tissue, or bathing of said organ or tissue in a storage medium which comprises said compound.

Claim 101 (new). A method of reducing or preventing cell death in a donor organ or tissue after it has been transplanted into a host due to the effects of reperfusion injury or due to the effects of host immune cells, comprising administering to said host in need thereof an effective amount of a compound having the Formula I:



or pharmaceutically acceptable salts or prodrugs thereof, wherein:

R<sub>1</sub> is an optionally substituted alkyl or hydrogen;

R<sub>2</sub> is hydrogen or optionally substituted alkyl;

R<sub>3</sub> is an alkyl, saturated carbocyclic, partially saturated carbocyclic, aryl, saturated heterocyclic, partially saturated heterocyclic or heteroaryl group, wherein said group is optionally substituted;

X is O, S, NR<sub>4</sub> or (CR<sub>4</sub>R<sub>5</sub>)<sub>n</sub>, where R<sub>4</sub> and R<sub>5</sub> are, at each occurrence, independently selected from the group consisting of hydrogen, alkyl and cycloalkyl, and n is 0, 1, 2 or 3; or

X is NR<sub>4</sub>, and R<sub>3</sub> and R<sub>4</sub> are taken together with the nitrogen atom to which they are attached to form a saturated heterocyclic, partially saturated heterocyclic or heteroaryl group, wherein said group is optionally substituted; or

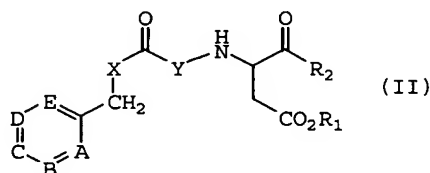
X is CR<sub>4</sub>R<sub>5</sub>, and R<sub>3</sub> and R<sub>4</sub> are taken together with the carbon atom to which they are attached to form a saturated carbocyclic, partially saturated carbocyclic, aryl, saturated heterocyclic, partially saturated heterocyclic or oxygen-containing heteroaryl group, wherein said group is optionally substituted; and

Y is a residue of a natural or non-natural amino acid;

provided that when X is O, then R<sub>3</sub> is not unsubstituted benzyl or *t*-butyl; and when X is CH<sub>2</sub>, then R<sub>3</sub> is not hydrogen.

Claim 102 (new). A method of reducing or preventing cell death in a donor organ or tissue after it has been transplanted into a host due to the effects of reperfusion

injury or due to the effects of host immune cells, comprising administering to said host in need thereof an effective amount of a compound having the Formula II:



or pharmaceutically acceptable salts or prodrugs thereof wherein:

R<sub>1</sub> is an optionally substituted alkyl or hydrogen;

R<sub>2</sub> is hydrogen or optionally substituted alkyl;

X is O, S, NR<sub>4</sub> or (CR<sub>4</sub>R<sub>5</sub>)<sub>n</sub>, wherein R<sub>4</sub> and R<sub>5</sub> are, at each occurrence, independently selected from the group consisting of hydrogen, alkyl, and cycloalkyl, and n is 0, 1, 2 or 3;

Y is a residue of a natural or non-natural amino acid;

A is CR<sub>6</sub> or nitrogen;

B is CR<sub>7</sub> or nitrogen;

C is CR<sub>8</sub> or nitrogen;

D is CR<sub>9</sub> or nitrogen;

E is CR<sub>10</sub> or nitrogen; provided that not more than three of A, B, C, D and E are nitrogen; and R<sub>6</sub>-R<sub>10</sub> independently are hydrogen, halo, C<sub>1</sub>-C<sub>6</sub> haloalkyl, C<sub>6</sub>-C<sub>10</sub> aryl, C<sub>4</sub>-C<sub>7</sub> cycloalkyl, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>2</sub>-C<sub>6</sub> alkenyl, C<sub>2</sub>-C<sub>6</sub> alkynyl, C<sub>6</sub>-C<sub>10</sub> aryl(C<sub>1</sub>-C<sub>6</sub>)alkyl, C<sub>6</sub>-C<sub>10</sub> aryl(C<sub>2</sub>-C<sub>6</sub>)alkenyl, C<sub>6</sub>-C<sub>10</sub> aryl(C<sub>2</sub>-C<sub>6</sub>)alkynyl, C<sub>1</sub>-C<sub>6</sub> hydroxyalkyl, nitro, amino, cyano, C<sub>1</sub>-C<sub>6</sub> acylamino, hydroxy, C<sub>1</sub>-C<sub>6</sub> acyloxy, C<sub>1</sub>-C<sub>6</sub> alkoxy, alkylthio, or carboxy; or one of R<sub>6</sub> and R<sub>7</sub>, or R<sub>7</sub> and R<sub>8</sub>, or R<sub>8</sub> and R<sub>9</sub>, or R<sub>9</sub> and R<sub>10</sub> are taken together with the carbon atoms to which they are attached to form a carbocycle or heterocycle, selected from the group consisting of —OCH<sub>2</sub>O—, —OCF<sub>2</sub>O—,

—(CH<sub>2</sub>)<sub>3</sub>—, —(CH<sub>2</sub>)<sub>4</sub>—, —OCH<sub>2</sub>CH<sub>2</sub>O—, —CH<sub>2</sub>N(R<sub>13</sub>)CH<sub>2</sub>—,

—CH<sub>2</sub>CH<sub>2</sub>N(R<sub>13</sub>)CH<sub>2</sub>—, —CH<sub>2</sub>N(R<sub>13</sub>)CH<sub>2</sub>CH<sub>2</sub>—, —N(R<sub>13</sub>)—CH=CH—, —CH=CH—

N(R<sub>13</sub>)—, —O—CH=CH—, —CH=CH—O—, —S—CH=CH—, —CH=CH—S—,

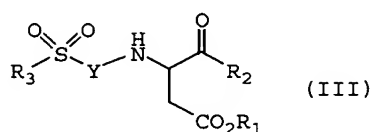
—N=CH—CH=CH—, —CH=N—CH=CH—, —CH=CH—N=CH—, —CH=CH—CH=N—, —N=CH—

CH=N—, and —CH=CH—CH=CH—; wherein R<sub>13</sub> is hydrogen, alkyl or cycloalkyl;



provided that when X is O, A is CR<sub>6</sub>, B is CR<sub>7</sub>, C is CR<sub>8</sub>, D is CR<sub>9</sub> and E is CR<sub>10</sub>, then at least one of the R<sub>6</sub>-R<sub>10</sub> is not hydrogen.

Claim 103 (new). A method of reducing or preventing cell death in a donor organ or tissue after it has been transplanted into a host due to the effects of reperfusion injury or due to the effects of host immune cells, comprising administering to said host in need thereof an effective amount of a compound having the Formula III:



or pharmaceutically acceptable salts or prodrugs thereof, wherein:

R<sub>1</sub> is an optionally substituted alkyl or hydrogen;

R<sub>2</sub> is hydrogen or optionally substituted alkyl;

R<sub>3</sub> is an alkyl, saturated carbocyclic, partially saturated carbocyclic, aryl, saturated heterocyclic, partially saturated heterocyclic or heteroaryl group, wherein said group is optionally substituted; and

Y is a residue of a natural or non-natural amino acid.